REMARKS

Claims 1 and 14 are amended and claims 20-31 are added to recite specific embodiments of the invention, as explained in more detail below. Claim 16 is canceled without prejudice or disclaimer. Applicants respectfully request entry of the amendments and reconsideration of claims 1, 14, 15 and 17-30 in view of the following remarks and the Rule 132 Declaration submitted concurrently herewith.

The Examiner Interview

Applicants thank Examiner Duffy for the courtesies extended during an interview, conducted on June 9, 2005, which was very helpful in advancing prosecution. Applicants' summary of the interview is set forth below.

The interview touched upon all of the issues raised in the pending Office Action. Applicants presented proposed claim amendments and presented a proposed Rule 132 Declaration believed to address the enablement issues and provide further evidence of the non-obviousness of the claimed invention. As reflected in the Interview Summary issued June 13, 2005, it was agreed that the proposed claim amendments and Declaration would obviate the prior art rejections. Applicants also believe that the proposed claim amendments and Declaration were found to overcome the enablement rejections.

Additional claim amendments were discussed during the interview, and these are reflected in the foregoing claim revisions. The Examiner also explained the type of showing that would obviate any concerns as to whether clinical trials of the claimed invention might constitute a prior public use of the invention. This information is provided below and supported by the accompanying Declaration.

Claim Amendments

Claim 1 is amended to recite a method of protecting an immune-compromised human from *Staphylococcal aureus* bacterial infection. The method comprises administering an immunoprotective amount of a vaccine comprising (i) a glycoconjugate of a Type 5 polysaccharide antigen of *S. aureus* and an immunocarrier and (ii) a glycoconjugate of a Type

8 polysaccharide antigen of *S. aureus* and an immunocarrier. Support for the recitation of an "immunoprotective amount" of the vaccine is found throughout the original specification, for example, at pages 5-6 and 21-23 (noting that the inventive methodology has been shown to protect immune-compromised patients from infection).

Claims 20-22 recite that the immunoprotective amount is sufficient to induce specific levels of Type 5 and Type 8 IgG antibodies at particular time periods post-vaccination. These embodiments are supported, for instance, at pages 20-24 (documenting achievement of the recited antibody levels). Table 1 and the publications cited at page 15 make clear that the antibody levels referenced in pages 20-24 are IgG antibody levels.

Claim 23 prescribes that the immunoprotective amount is sufficient to provide protection at 40 weeks post-vaccination. Relevant support appears in the specification at page 23.

Claims 24 and 25 recite that the vaccine comprises (about) 100 μg of the Type 5 glycoconjugate and (about) 100 μg of the Type 8 glycoconjugate. These embodiments of the invention are supported, for example, at page 14 of the specification as filed, which teaches that 1 mL of a vaccine comprising 100 μg/mL of each antigen was used. Although the specification does not expressly state that the vaccine comprises "about" 100 μg of each glycoconjugate, those skilled in the art reading the specification will understand that the amount given is approximate. Applicants note further that by "about" they intend to encompass vaccines comprising 100 μg +/- 20% of each antigen (i.e., 80-120 μg), which is consistent with the variation permitted in the IND application for the vaccine.

Claims 26-30 recite specific patient populations. These embodiments are supported, for example, at page 5, 11 and 16 (diabetic patients), page 16 (patients with vascular graft access), page 11 (elderly patient in an extended care facility), pages 1 and 12 (invasive surgical procedure patients), and original claim 14 (patient in acute care setting).

Claim 31 recites that the vaccine is administered without an adjuvant. This embodiment of the invention is supported, for example, at page 11 of the specification.

Enablement Rejection

The Office Action questioned whether, in light of data in the specification relating to ESRD patients, the claimed invention is enabled with respect to immune-compromised patients generally. As discussed during the Interview, the Rule 132 Declaration submitted herewith evidences that data demonstrating the efficacy of the claimed invention in ESRD patients are reasonably predictive of efficacy in immune-compromised patients generally. This is so because ESRD patients exhibit a number of deficiencies in their immune system and are representative of immune compromised patients generally, including elderly patients (*i.e.*, patients aged 55 and older), diabetic patients, and patients with invasive surgical procedures (including patients with vascular graft access and implants). For example, ESRD patients, the elderly, diabetic patients, hemodialysis patients, and patients with uremia all may exhibit inactive complement and ineffective neutrophils. Thus, the immune deficiencies exhibited by ESRD patients are similar to the immune deficiencies exhibited by other immune compromised patient populations, and ESRD patients are representative of immune compromised patients generally.

Additionally, because of the specific patient population of the trial described in Example 2 of the application, the data in the application demonstrating efficacy in ESRD patients also directly establishes the efficacy of the invention in diabetic patients, elderly patients, and patients with invasive surgical procedures. As set forth in the Rule 132 Declaration:

- The mean patient age was 58.3 years, and 1,111 of the 1804 patients followed were aged 55 or older. Moreover, the data for patients over age 65 in the study shows that the vaccine is effective in those patients.

- 52% of the StaphVAX group and 51% of the placebo group were diabetic (in total, 931 of the 1804 patients followed were diabetic), and at all times from weeks 3 to 54 post-vaccination, the cumulative number of patients with bacteremia was greater for the diabetic placebo group than for the diabetic StaphVAX group.

- 69% of the subjects in both the StaphVAX and placebo groups had vascular graft access (*i.e.*, had undergone invasive surgical procedures). Indeed all of the patients had some type of vascular access, either with grafts or fistulas. Thus, the data reported in the specification demonstrates the efficacy of the invention in patients who

have undergone invasive surgical procedures. Also, as set forth in the Declaration, the inventors conducted a study in a rabbit knee model to confirm the efficacy of the invention in patients who have undergone the invasive surgical procedure of receiving an orthopedic implant. All animals in the StaphVAX group achieved an antibody titer at least 10-fold higher than baseline, and animals in the StaphVAX group demonstrated a significant decreased incidence of infection compared to controls.

Accordingly, Applicants have demonstrated that the specification enables the full scope of the claims. Reconsideration and withdrawal of the enablement rejections are therefore respectfully requested.

Prior Art Rejections

The instant claims recite a method of protecting an immune-compromised human from *Staphylococcal aureus* bacterial infection by administering an immunoprotective amount of a vaccine comprising (i) a glycoconjugate of a Type 5 polysaccharide antigen of *S. aureus* and an immunocarrier and (ii) a glycoconjugate of a Type 8 polysaccharide antigen of *S. aureus* and an immunocarrier. As discussed during the interview and as set forth in the Rule 132 Declaration, the prior art does not teach or suggest such a method.

The Rule 132 Declaration evidences that the clinical trial referenced in the prior art cited in the Office Action did not involve the administration of an amount of Type 5/Type 8 glycoconjugate vaccine that was immunoprotective in immune-compromised patients, as claimed. Instead, the clinical trial was deemed to be unsuccessful because protection was not achieved in the ESRD patients. In other words, it is only the instant application and not the prior art that teaches administering an amount of Type 5/Type 8 glycoconjugate vaccine that is effective to induce the quality and quantity of antibodies required for protection in immune-compromised patients. The Declaration also evidences that, at the time the instant application was filed, it would not have been obvious that any amount of Type 5/Type 8 glycoconjugate vaccine would prove to be immunoprotective in immune-compromised patients.

Because the claimed invention is not taught or suggested by the prior art, the § 102 and § 103 rejections should be withdrawn.

Clinical Trials/Public Use

The Office Action raises a question as to whether the clinical trial referenced in the cited prior art might constitute a prior "public use" of the claimed invention. As discussed above, however, and as shown in the Rule 132 Declaration, that clinical trial was not a prior use of the claimed invention.

The data reported in the application were obtained from a clinical trial of the claimed invention. As shown below, that clinical trial was not a prior "public use" of the claimed invention under § 102(b).

Circumstances to consider when determining whether a clinical trial constituted a public use include: "the nature of the activity that occurred in public; the public access to and knowledge of the public use; whether there was any confidentiality obligation imposed on persons who observed the use; whether persons other than the inventor performed the testing; the number of tests; the length of the test period in relation to tests of similar devices; and whether the inventor received payment for the testing." *See Janssen Pharm., N.V. v. Eon Labs Mfg., Inc.*, 2005 WL 1384230, *4 (Fed. Cir. June 13, 2005) (non-precedential; copy appended), *citing Allied Colloids, Inc. v. Am. Cyanamid Co.*, 64 F.3d 1570, 1574 (Fed. Cir. 1995). Relevant characteristics of a clinical trial may include whether the trial was blinded or double-blinded and what control the inventors and/or assignees exercised over the trial (*i.e.*, whether they drafted the protocols, selected investigators, conducted site visits, or participated in, supervised or reviewed the results of the trial). *See, e.g., Smithkline Beecham, Corp. v. Apotex Corp.*, 286 F.Supp. 2d 925, 932-933, 934 (N.D. Ill. 2001) (copy attached).

When evaluated under these criteria, the clinical trial reflected in the application does not constitute a "public use" of the invention that might create a statutory bar to patentability. As set forth in the Declaration, and as supported by the documents included in Appendix C thereto, the clinical trial of the invention was designed by the assignee of the application, and was conducted under its direction and control. The clinical trial was a randomized, placebo-controlled, double-blind study. Investigators were required to sign confidentiality agreements and were required to sign an agreement stating that they would follow the detailed protocol

designed by the assignee. Under the protocol, neither the investigators nor the patients knew whether a given patient received the vaccine or a placebo. In view of these restrictions, the clinical trial did not constitute a "public use" of the invention. *See, e.g., Smithkline Beecham*, 286 F.Supp. 2d at 932, 934.

CONCLUSION

Applicants believe that the application now is in condition for allowance, and an early notice to that effect is earnestly solicited. Should there be any questions regarding this submission, or should any issues remain, the Examiner is invited to contact the undersigned by telephone in order to advance prosecution.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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